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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/807,720	04/18/2001	Henry Daniell	1462- PCT-US-00	4039

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EXAMINER
KUBELIK, ANNE R

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 03/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/807,720	DANIELL, HENRY	
	Examiner	Art Unit	
	Anne R. Kubelik	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 January 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10,12,13 and 15-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10, 12-13 and 15-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *with the application* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Claims 11 and 14 have been cancelled and claims 1-10, 12-13 and 15-18 have been amended, as requested in Paper No. 10, filed 14 January 2003. Claims 1-10, 12-13 and 15-18 are pending.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. The amendment filed 14 January 2003 to pg 12 of the specification is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material that is not supported by the original disclosure is as follows: changing the sequences of the primer that anneals to the 5' end and the primer that anneals to the 3' end of 16SrDNA.

Applicant is required to cancel the new matter in the reply to this Office Action.

4. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required. In the response filed 14 January 2003 Applicant urges that a copy of pg 19 was enclosed (response pg 5). This is not found persuasive, because it was not so enclosed.

Response to Amendment

5. The objection to claims 16-17 under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim may not depend from another multiple dependent claim is WITHDRAWN in light of amendment to the claims.

6. The objection to claims 1-18 because of informalities is WITHDRAWN in light of amendment to the claims.

Claim Objections

7. Claims 1, 6, 8-10 and 12-13 are objected to because of the following informalities:

There should be a comma before "which" in line 2 of claim 1.

There should be a comma before "wherein" in line 1 of claims 6, 8-10 and 12-13.

An article is missing before "maize" in claim 10, line 2.

Claim Rejections - 35 USC § 112

8. Claims 1-10, 12-13 and 15-18 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The rejection is repeated for the reasons of record as set forth in the Office action mailed 5 January 2002, as applied to claims 1-18. Applicant's arguments filed 14 January 2003 have been fully considered but they are not persuasive.

Applicant urges that the specification teaches plastid transformation vectors that encode cytotoxic antimicrobial peptides. Applicant urges that AMPs are well described by a number of references incorporated by reference into the specification (response pg 5-6).

This is not found persuasive because the components of the claimed vectors are not described. Even the vector used in the example is not adequately described; the sequence of the nucleic acid encoding the AMP is not described and the "flanking sequences" are not described.

Applicant urges that the unique feature is not the peptide AMPs but is stably integrating a gene encoding an AMP into the plastid genome of a plant cell, wherein the AMP is transcribed in the plastid and transferred into the cytosol when a microbe infects the plant cell (response pg 6).

This is not found persuasive because for the vector to be described and for the plants transformed with the vector to be described, the components of the vector must be described.

Applicant urges that by describing and disclosing a particular amino acid sequence, they have specifically defined the genes and DNA sequences that are capable of coding for the desired amino acid sequences. Applicant urges that the specification on pg 3 discusses the unique sequence features of AMPs, which Applicant urges allows one of skill in the art to find all of the various amino acid sequences that comprise AMPS, and their resulting DNA sequences. Applicant urges that one of skill in the art could readily ascertain whether a homologous amino acid sequence was an AMP. Applicant urges that they need not show every AMP, or that other invention operates with every AMP, provided it operates with the AMPs tested and that other AMPs are sufficiently similar in structure that one of skill in the art would be lead to believe those other AMPs would work in Applicant's invention (response pg 6-7).

This is not found persuasive because description of the features of a protein does not provide a description of the nucleic acid that encodes that protein. See *Fiddes v. Baird* (BdPatApp&Int) 30 USPQ2d 1481, which states "knowledge of [the] amino acid sequence of [a] protein, coupled with [the] established relationship in genetic code between [a] nucleic acid and [the] protein it encodes, would not establish inventor's possession of [a] gene encoding that protein".

Applicant urges that antibiotic-free selectable markers in plants are well-known, as evidenced by a US Patent, not included in the response. Furthermore, Applicant urges that the particular antibiotic-free selectable marker is a matter of choice (response pg 7).

This is not found persuasive because antibiotic-free selectable markers that function in plastids are not described. The patent could not considered because it was not sent.

9. Claims 1-10, 12-13 and 15-18 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The rejection is repeated for the reasons of record as set forth in the Office action mailed 5 January 2002, as applied to claims 1-18. Applicant's arguments filed 14 January 2003 have been fully considered but they are not persuasive.

Applicant urges that the specification teaches plastid transformation vectors that are stably integrated into a variety of plant species, plants so transformed and a method of making them and that the invention can be practiced without undue experimentation. Applicant urges that on pg 9 such a vector is clearly set forth, comprising sequences well-known and available to one of skill in the art (response pg 7-8).

This is not found persuasive because the specification on pg 9 does not teach the components of the vector. Figure 1 supposedly illustrates the petunia flanking sequence used, however, it consists only of a drawing and a peptide sequence and contains no DNA sequences.

Applicant also urges that several references and patents, all not sent with the response, describe plastid transformation vectors and that a number of chloroplast genomes have been sequenced and are available in GenBank (response pg 8-11).

This is not found persuasive because the instant specification fails to teach transformation of the plastids of any other plant species, including maize, rice, grass, rye, barley, oats, wheat, soybean, peanut, grape, sweet potato, pea, canola, tomato or cotton. The specification also fails to teach any plastid transformation vector that is "universal" and that has flanking sequences that are homologous to spacer sequences that are conserved in the plastid genomes of different plant

species. The specification also fails to teach selectable marker sequences that allow selection in plastids in the absence of an antibiotic.

The cited references could not considered because they were not sent.

Furthermore, as discussed in the prior Office action, the region of the tobacco plastid genome commonly used for targeting of transformation vectors is not present in the same configuration in the plastid genomes of other economically important plants; for example, rice (Kanno et al, 1993, Curr. Genet. 23:166-174) lacks the orf131/orf70B gene (see Figure 3). The specification fails to teach a region of the plastid genome that is homologous across all plant species.

Applicant urges that DeGray et al, enclosed, demonstrates the expression of MSI-99 in transformed plastids. Applicant urges that Okamoto et al and Allefs et al, cited in the prior Office action, teach insertion of an AMP into the nuclear genome of plants, which negatively affected their ability to be transcribed and retained in the cytosol (response pg 11).

This is not found persuasive Okamoto et al and Allefs et al teach that the expression of other antimicrobial proteins is unpredictable. The specification and DeGray et al only show that MSI-99 can be expressed and do not overcome the unpredictability of other AMPs.

Applicant urges that their invention involves transcribing and retaining the peptide within the chloroplast genome until release is necessary (response pg 11).

This is not found persuasive because the claims are not directed to this. However, an amendment to do so would not enable the invention, for the reasons indicated above.

10. Claims 1-10, 12-13 and 15-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that

Applicant regards as the invention. Dependent claims are included in all rejections. The rejection is repeated for the reasons of record as set forth in the Office action mailed 5 January 2002, as applied to claims 1-18. Applicant's arguments filed 14 January 2003 have been fully considered but they are not persuasive.

Applicant urges that the claims have been amended to address these issues (response pg 12-13). This is not found persuasive because the following rejections remain or are new, due to amendment:

It is not clear in claim 1, if the phrase starting with 'which" in line 2 is intended to modify "plastid" or "vector". By position in the claim it modifies "plastid". If Applicant intended it to modify "vector", it is suggested that 'which " be replaced with --, wherein the vector--.

Claim 1 lacks antecedent basis for the limitations "the plastid genome" in line 7 and "the flanking sequence" in lines 8-9.

Claim 3 is indefinite in its recitation of the abbreviation "PGLa", which is not defined in the specification.

Claim 5 is indefinite in its recitation of "wherein the selectable marker sequence is not an antibiotic selectable marker". Applicant appears to be equating a DNA sequence with what it encodes.

In claim 6 it is unclear what it means for a vector to be competent for stably transforming something. Vectors are not competent for transformation; the cells into which they are transformed are made competent for transformation.

In claim 6, line 2, it appears that all the plant species share a single plastid.

Claim 6 is indefinite in its recitation of "the heterologous DNA coding sequence is conserved in the plastid solanaceous, monocotyledonous or dicotyledonous plant species." This

phrase makes no sense. How can the heterologous DNA sequence be in plastids, much less conserved in them? What is a plastid solanaceous?

In claim 7 products must be claimed in the alternative. One cannot claim plants and progeny, but plants or progeny are acceptable.

Claim 13 lacks antecedent basis for the limitation "the transformed plastid of the plant and subsequent generations of the stably transformed plant". Additionally, it appears that all the plants share a single plastid.

Claim 13 is indefinite in its recitation of "are can" in line 3. Are words missing?

Claim 15 lacks antecedent basis for the limitations "an integration and expression vector of claims 1, 2, 3, 4, 5 or 6" in lines 2-3.

Claim 16 is indefinite in its recitation of "and in the prevention of the spread of infection by the target bacteria." This phrase grammatically does not go with the rest of the claim. It is also unclear what is doing the preventing.

It is not clear in claims 17 and 18 where the rbs and the 5' UTR are located relative to the other components of the vector. Applicant urges that one of skill in the art would know how to locate these areas on a plastid and Applicant is merely claiming that the vector further comprises RBS and a 5'UTR (response pg 13). This is not found persuasive because describing the claimed vector requires one knows where the components of that vector are located. Are these components even operably linked to anything else in the vector?

It is unclear in claim 15 what is involved in allowing a plant to control phytopathogenic bacteria.

Claim Rejections - 35 USC § 103

11. Claims 1-10, 12-13 and 15-18 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Maliga et al (US Patent 5,877,402, filed January, 1994) in view of Davies et al (WO 90/11770). The rejection is repeated for the reasons of record as set forth in the Office action mailed 5 January 2002, as applied to claims 1-18. Applicant's arguments filed 14 January 2003 have been fully considered but they are not persuasive.

Applicant urges that Malaga et al teaches away from the insertion of a gene encoding an AMP. Applicant urges that nothing in Maliga et al discloses that foreign proteins expressed in a plastid could function outside of plastids. Applicant urges that in the past no protein was shown to be produced inside the chloroplast and subsequently successfully exported so that it would function outside the chloroplast (response pg 13-14).

This is not found persuasive.

In response to applicant's argument that the references fail to show certain features of Applicant's invention, it is noted that the features upon which Applicant relies (*i.e.*, production of a protein inside the chloroplast and subsequently exportation so that it would function outside the chloroplast) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

It is noted however, that Maliga et al teach that GUS produced in transformed chloroplasts works outside the plants, in protein extracts (column 61, lines 49-54); thus proteins produced in the chloroplast do function when outside the chloroplast.

Applicant also urges that the recitation in the 112, 1st, enablement rejection that expressing pesticidal peptides is unpredictable is consistent with the prior art belief that AMPs

could not function properly within plants. Applicant urges that the prior art believed that AMPs were not stable inside living prokaryotes and would therefore be unstable inside plastids (response pg 14-15).

This is not found persuasive. Applicant provides no evidence for the assertion that the prior art believed that AMPs were not stable inside living prokaryotes and would therefore be unstable inside plastids or that no AMP was ever expressed in plants.

Applicant urges that Davies et al does not teach a Brassica plant transformed with a vector encoding defensin or magainin, but merely teaches a vector that is introduced into Agrobacteria and into Brassica plants for only a single generation. Applicant also urges that Davies et al do not teach plastid transformation. Applicant urges that the eukaryotic regulatory sequences taught by Davies would not be functional in plastids and Agrobacterium-mediated transformation teaches away from plastid transformation (response pg 15-16).

This is not found persuasive. Davies teaches that at least some AMPs can be expressed within plants. Maliga et al teaches all the vector components and methods for plastid transformation and provides motivation to combine.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

12. Claims 1-10, 12-13 and 15-18 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Maliga et al (US Patent 5,877,402, filed January, 1994) in view of Smith et al (WO 99/06564). The rejection is repeated for the reasons of record as set forth in the Office

action mailed 5 January 2002, as applied to claims 1-18. Applicant's arguments filed 14 January 2003 have been fully considered but they are not persuasive.

Applicant urges that Smith only states that an AMP could be expressed in plastids, but urges that the regulatory sequences taught by Smith et al would not be functional in plastids. Applicant also urges that the vectors taught by Smith et al would not function in plastid transformation. Applicant urges that it would not be obvious to one of ordinary skill in the art to transform a plant plastid with a vector encoding an AMP because DNA delivery methods required for plastid transformation are different than those required for nuclear transformation (response pg 16-17).

This is not found persuasive. Smith teaches nucleic acids encoding AMPs and suggests expressing them in plastids. Maliga et al teaches all the vector components and methods for plastid transformation. Thus, all components of Applicant's invention are taught by the prior art.

In response to Applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Conclusion

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (703) 308-5059. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at (703) 306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Customer Service at (703) 308-0198.

Anne R. Kubelik, Ph.D.
March 20, 2003

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